Cerebro-facio-thoracic dysplasia

Cerebro-facio-thoracic dysplasia is a rare condition characterized by abnormal development (dysplasia) of the brain (cerebro) and structures in the face (facio) and torso (thoracic). The problems with development lead to the key features of cerebro-facio-thoracic dysplasia, which include severe intellectual disability, distinctive facial features, and abnormalities of the ribs and spinal bones (vertebrae).

In addition to intellectual disability, individuals with cerebro-facio-thoracic dysplasia have delayed development of speech and movement (motor) skills, and in some, these skills never develop. Nearly one-quarter of affected individuals never learn to speak and almost half are unable to walk. Weak muscle tone (hypotonia) and difficulty feeding occur in some affected infants. People with cerebro-facio-thoracic dysplasia can have behavioral problems, such as anxiety, autism spectrum disorder, or self-injuring behavior; however, many people with the condition are described as friendly and good-natured.

Distinctive facial features common in cerebro-facio-thoracic dysplasia include a wide, short skull (brachycephaly); highly arched eyebrows or eyebrows that grow together in the middle (synophrys); widely spaced eyes (hypertelorism); a wide nasal bridge; low-set ears; an upper lip with pronounced curves (Cupid's bow upper lip); and small teeth (microdontia). Some affected individuals have overgrowth of the gums (gingival hyperplasia), an opening in the roof of the mouth (cleft palate), or a split in the upper lip (cleft lip).

Problems with bone development in the torso (thorax) commonly leads to bone abnormalities such as two or more ribs that are joined together (fused) or ribs that are abnormally shaped with two prongs at one end (bifid ribs). Many people with cerebro-facio-thoracic dysplasia have abnormal side-to-side curvature of the spine (scoliosis) due to malformation of the vertebrae; some vertebrae may also be fused. Additionally, the shoulder blades can be affected in people with this condition.

A wide variety of other features can occur in cerebro-facio-thoracic dysplasia, such as abnormalities involving the eyes, skin, or hair. Heart defects, digestive problems, or genitourinary problems (such as abnormal kidneys or reproductive organs) can also occur. Affected individuals may also have bone or joint abnormalities in other parts of the body.

Frequency

Cerebro-facio-thoracic dysplasia is a rare disorder. Its prevalence is unknown.

Causes

Cerebro-facio-thoracic dysplasia is caused by mutations in a gene called *TMCO1*. This gene provides instructions for making a protein that forms specialized structures called channels through which positively charged calcium atoms (calcium ions) flow. The protein is found in the membrane of a cell structure called the endoplasmic reticulum, which acts as a storage center for calcium ions. When there is too much calcium in the endoplasmic reticulum, four TMCO1 proteins come together to form a channel that releases the excess calcium into the surrounding fluid inside the cell (cytoplasm). Calcium acts as a signal for many cellular functions including control of cell growth and division and gene activity. The proper balance of calcium ions in cells and cell compartments is important for the development and function of various tissues and organs.

TMCO1 gene mutations result in a shortage of TMCO1 proteins. Without this protein, TMCO1 channels cannot form, and excess calcium builds up in the endoplasmic reticulum. The imbalance of calcium ions disrupts development of the brain and structures in the head, face, and torso, resulting in the features of cerebro-facio-thoracic dysplasia.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- cerebrofaciothoracic dysplasia
- CFSMR
- CFTD
- craniofacial dysmorphism, skeletal anomalies, and mental retardation syndrome
- Pascual-Castroviejo syndrome
- TMCO1 defect syndrome

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Craniofacial dysmorphism, skeletal anomalies, and mental retardation syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1859252/

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Craniofacial Abnormalities
  https://medlineplus.gov/craniofacialabnormalities.html
- Health Topic: Developmental Disabilities
  https://medlineplus.gov/developmentaldisabilities.html

Genetic and Rare Diseases Information Center

- Cerebro facio thoracic dysplasia
  https://rarediseases.info.nih.gov/diseases/1210/cerebro-facio-thoracic-dysplasia

Additional NIH Resources

- Eunice Kennedy Shriver National Institute of Child Health and Human Development: Intellectual and Developmental Disabilities
  https://www.nichd.nih.gov/health/topics/idds/conditioninfo/default

Educational Resources

- Hassenfeld Children's Hospital at New York University Langone: Types of Developmental Delays in Children
  https://nyulangone.org/conditions/developmental-delays-in-children/types
- MalaCards: craniofacial dysmorphism, skeletal anomalies, and mental retardation syndrome
  https://www.malacards.org/card/craniofacial_dysmorphism_skeletal_anomalies_and_mental_retardation_syndrome
- Merck Manual Consumer Version: Intellectual Disability
  https://www.merckmanuals.com/home/children-s-health-issues/learning-and-developmental-disorders/intellectual-disability
- Orphanet: Cerebrofaciothoracic dysplasia
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1394

Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities
  http://aaidd.org/intellectual-disability/definition
- Children's Craniofacial Association
  https://ccakids.org/
- Foundation for Faces of Children
  https://facesofchildren.org/

- Resource List from the University of Kansas Medical Center: Facial Anomalies / Craniofacial Conditions
  http://www.kumc.edu/gec/support/craniofa.html
- The Arc: For People with Intellectual and Developmental Disabilities
  https://www.thearc.org/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28cerebro-facio-thoracic+dysplasia%5BTIAB%5D%29+OR+%28cerebrofaciothoracic+dysplasia%5BTIAB%5D%29+OR+%28TMCO1+defect%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- CRANIOFACIAL DYSMORPHISM, SKELETAL ANOMALIES, AND MENTAL RETARDATION SYNDROME
  http://omim.org/entry/213980

Medical Genetics Database from MedGen

- Cerebro-facio-thoracic dysplasia
  https://www.ncbi.nlm.nih.gov/medgen/929616
- Craniofacial dysmorphism, skeletal anomalies, and mental retardation syndrome
  https://www.ncbi.nlm.nih.gov/medgen/347111

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https://ghr.nlm.nih.gov/condition/cerebro-facio-thoracic-dysplasia

Reviewed: March 2019
Published: April 30, 2019

Lister Hill National Center for Biomedical Communications
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National Institutes of Health
Department of Health & Human Services